Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Bortezomib in multiple myeloma and lymphoma.

Bibliographic Source(s)

Kouroukis CT, Reece D, Baldassarre FG, Haynes AE, Imrie K, Cheung M, Hematology Disease Site Group. Bortezomib in multiple myeloma and lymphoma. Toronto (ON): Cancer Care Ontario (CCO); 2013 Mar 18. 209 p. (Evidence-based series; no. 6-18). [293 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Reece D, Kouroukis T, Haynes AE, Imrie K. Bortezomib in multiple myeloma and lymphoma. Toronto (ON): Cancer Care Ontario (CCO); 2008 Nov 24. 41 p. (CED-CCO special advice report; no. 11).

The EVIDENCE-BASED SERIES report, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

Recommendations

Major Recommendations

Question 1. Efficacy of Bortezomib

Multiple Myeloma (MM): Previously Untreated Patients

Patients Who Are Ineligible for Autologous Stem Cell Transplantation (ASCT)

For patients with previously untreated MM who are ineligible for ASCT, the combination of bortezomib, melphalan, and prednisone is a recommended first-line treatment option and preferred over treatment with melphalan and prednisone alone. The recommended dose and schedule of bortezomib is 1.3 mg/m^2 given as a rapid intravenous bolus over 3 to 5 seconds on days 1, 4, 8, 11, 22, 25, 29, and 32 during cycles 1 to 4 and on days 1, 8, 22, and 29 during cycles 5 to 9. Melphalan 9 mg/m^2 and prednisone 60 mg/m^2 are to be given on days 1 through 4 of a six-week cycle. A total of nine cycles is given.

Patients Who Are Candidates for ASCT

In patients with previously untreated MM, a recommended option is the use of bortezomib in combination with dexamethasone or other immunomodulatory or alkylating agents as induction therapy prior to ASCT, and it is preferred over induction therapy without novel agents (i.e., dexamethasone alone or vincristine, doxorubicin and dexamethasone [VAD]). The recommended dose and schedule of bortezomib should be 1.3 mg/m^2 given as a rapid intravenous bolus over 3 to 5 seconds days 1, 4, 8, and 11 of four 3-week cycles.

Multiple Myeloma: Patients with Relapsed/Refractory Disease

- The combination of bortezomib and pegylated liposomal doxorubicin (PLD) is a recommended treatment option for patients with MM that has relapsed or is refractory to previous treatment who are candidates for further chemotherapy; who have no clinically significant cardiac disease; who have received less than 240 mg/m^2, or the equivalent cumulative dose of doxorubicin; who have a left ventricular ejection fraction in the normal range; and who would be expected to tolerate the myelosuppression of combination therapy. The recommended dose and schedule of bortezomib is 1.3 mg/m^2 given as a rapid intravenous bolus over three to five seconds on days 1, 4, 8, and 11 of an every-21-days cycle. PLD 30 mg/m^2 is administered as a one-hour infusion on day 4 of each cycle. Treatment should be continued for eight cycles unless disease progression or unacceptable treatment-related toxicity occurs. Patients who are still responding and who are tolerating therapy well may continue until the criteria of progressive myeloma are met, i.e., at least a 25% increase in the serum monoclonal protein level (which must be an absolute minimum increase of 5 g/L). The treatment can be discontinued two to four cycles after the achievement of complete remission (CR) (as determined by negative electrophoresis and immunofixation).
- For patients with MM refractory or relapsed to previous treatment, who are candidates for further chemotherapy but are not candidates for the combination of bortezomib and PLD, bortezomib monotherapy is recommended as a preferred treatment option. The recommended dose and schedule of bortezomib is 1.3 mg/m^2, given as a rapid intravenous bolus over three to five seconds on days 1, 4, 8, and 11 for eight three-week cycles, and then on days 1, 8, 15, and 22 for three five-week maintenance cycles.

Lymphoma (Including Waldenström's Macroglobulinemia)

For patients with relapsed or refractory mantle cell lymphoma, bortezomib monotherapy is a reasonable treatment option. Bortezomib should be administered at a dose of 1.3 mg/m^2 given as a rapid intravenous bolus over three to five seconds on days 1, 4, 8, and 11 of a 21-day cycle. Treatment should continue until disease progression or intolerance, or until two to four cycles after maximal response has been achieved.

Question 2. Toxicity

- A complete blood count is recommended with blood chemistries, including electrolytes and creatinine levels, all to be monitored at minimum on days 1 and 8 of each cycle. The dose of bortezomib should be reduced or held immediately for the development of painful neuropathy, as described in the product monograph; dose modification may also be required for peripheral sensory neuropathy without pain, or other toxicities.
- In lymphoma, a weekly bortezomib (alone or in combination) schedule is preferable to a bi-weekly schedule to prevent excess toxicity.
- Because bortezomib is fatal if administered intrathecally, the recommendation is to administer it only by the approved intravenous or subcutaneous routes.

Question 3. Patient Subgroups That Are More or Less Likely to Benefit from the Use of Bortezomib

In MM, treatment with bortezomib combinations (i.e., bortezomib with melphalan and prednisone for newly diagnosed patients, or either bortezomib and dexamethasone or bortezomib and pegylated liposomal doxorubicin for those with relapsed or refractory disease) is recommended for all patient subgroups (i.e., patients who are older, patients with impaired renal function, patients with a high-risk cytogenetic profile, patients exposed to multiple previous lines of therapy and ASCT, and patients with an elevated level of β2-microglobulin).

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Multiple myeloma
- Lymphoma
- Waldenström's macroglobulinemia

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Hematology

Internal Medicine

Oncology

Intended Users

Advanced Practice Nurses

Health Care Providers

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To evaluate the efficacy of bortezomib alone or in combination as measured by survival, quality of life, disease control (e.g., time-to-progression [TTP]), response duration, or response rate in patients with multiple myeloma, or lymphoma, including Waldenström's macroglobulinemia
- To evaluate the toxicity associated with the use of bortezomib
- To determine which patients are more or less likely to benefit from treatment with bortezomib

Target Population

Adult patients with multiple myeloma, or lymphoma of any type, stage, histology, or performance status

Interventions and Practices Considered

Bortezomib alone or in combination with other agents

Major Outcomes Considered

- Survival
- Time-to-progression/progression-free survival
- Response duration
- Response rate
- Quality of life

- Toxicity

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Strategy

MEDLINE (Ovid) (October 2004 through August 2012), EMBASE (Ovid) (2004 Week 42 through August 27, 2012), and the Cochrane Library (August 2012) databases were searched. The search strategies for MEDLINE and EMBASE are shown in Appendix 2 of the original guideline. The search strategies were adapted for the Cochrane database.

In addition, the Working Group members' personal files and conference proceedings of the American Society of Clinical Oncology (ASCO) (2005-2012) and the American Society of Hematology (ASH) (2005-2011) were searched for relevant trials. The following Web sites were also searched for existing evidence-based practice guidelines:

- Canadian Medical Association Infobase (https://www.cma.ca/en/Pages/cma_default.aspx#)
- National Guideline Clearinghouse (http://www.guideline.gov/)
- National Institute for Health and Care Excellence (http://www.nice.org.uk/)

Relevant articles and abstracts were selected and reviewed by two reviewers, and the reference lists from these sources were searched for additional trials.

Study Selection Criteria

Multiple Myeloma (MM)

Inclusion Criteria

Articles were selected for inclusion in this systematic review of the evidence if they were published full report articles or published meeting abstracts of:

- Systematic reviews (only of full report articles), meta-analyses, or evidence-based clinical practice guidelines of bortezomib in adult patients with MM
- Randomized studies including adult patients with MM and evaluating bortezomib as a single agent or in combination with other regimens
- Trials could compare bortezomib to any agent, any combination of agents, or placebo
- Trials reporting one or more of the following outcomes: survival, quality of life, disease control (e.g., time-to-progression [TTP]), response duration, response rate, or adverse effects

Exclusion Criteria

Studies were excluded if they were:

- Letters, comments, books, notes, editorial publication types, or abstract publication of systematic reviews
- Articles published in a language other than English, due to the cost of translations
- Clinical practice guidelines without a description of a systematic literature search

Lymphoma

Inclusion Criteria

Articles were selected for inclusion in this systematic review of the evidence if they were published full report articles or published meeting abstracts of:

- Systematic reviews (only full report articles), meta-analyses, or evidence-based clinical practice guidelines of bortezomib in adult patients with Waldenström's macroglobulinemia (WM) or lymphoma
- Studies including adult patients with WM or lymphoma (any histologic subtype, stage, performance status, or disease type)
- Randomized trials in which bortezomib could be compared with any agent, any combination of agents, or placebo
- Single-arm phase II trials evaluating bortezomib as a single agent or in combination with other regimens
- Trials reporting one or more of the following outcomes: survival, quality of life, disease control (e.g., TTP), response duration, response rate, or adverse effects

Exclusion Criteria

Studies were excluded if they were:

- Letters, comments, books, news, editorial publication types, or abstract publication of systematic reviews
- Single-arm phase II trials reporting fewer than 20 patients (all disease types combined)
- Abstract reports of single-arm phase II trials that have not been previously fully published
- Phase I trials
- Clinical practice guidelines without a description of a systematic literature search

Abstracts that were reports of interim analyses, as well as abstracts of non-comparative studies, (as per Program in Evidence-based Care [PEBC] policy) and systematic reviews that were more than two years old were also not included.

The methodologist screened the titles and the abstracts of the citations identified by the electronic databases and the titles of the abstracts from ASCO and ASH conference proceedings and excluded the citations that reported on studies that did not investigate the use of bortezomib or that did not meet the inclusion criteria for design (i.e., were not randomized trials or were not systematic reviews for MM or were retrospective studies for lymphoma). The full texts of the remaining articles were retrieved in the library, and two authors for myeloma and two authors for lymphoma reviewed them against the selection criteria.

Number of Source Documents

Multiple Myeloma

A total of 26 unique studies (6 systematic reviews, 17 unique randomized controlled trials [RCTs], and 3 guidelines) and 40 companion publications were included.

Lymphoma and Waldenström's Macroglobulinemia

A total of 28 unique studies (1 Phase III RCT, 3 randomized Phase II trials, 23 Phase II single arm studies, and 1 abstract of interim analysis) and 7 companion publications were included.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Quality Assessment

For the evaluation of the quality of included randomized controlled studies (RCTs), the Working Group considered discrete parameters such as the reporting of the sample-size calculation for the study, randomization method, allocation concealment, blinding, intention-to-treat (ITT) analysis, final analysis, early termination, losses to follow-up, and ethical approval. The Group did not perform quality assessments of single-arm phase II studies.

Synthesizing the Evidence

Data appropriate for meta-analysis were not expected but would be investigated if such data are found. In the case of a meta-analysis, for planned analyses, the primary outcome of interest is progression-free survival (PFS) and the secondary outcomes of interest are response rate and overall survival; subset analyses will be conducted by histology. In case the heterogeneity of the studies does not allow for statistical pooling, a narrative synthesis will be presented; the studies will be grouped by patient characteristics of untreated multiple myeloma (MM) disease and relapsed or refractory disease.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The evidence-based series (EBS) guidelines developed by the Program in Evidence-based Care (PEBC), Cancer Care Ontario (CCO), use the methods of the Practice Guidelines Development Cycle. For this project, the core methodology used to develop the evidentiary base was the systematic review. Evidence was selected and reviewed by two members of the PEBC Hematology Disease Site Group (DSG) and one methodologist.

The systematic review is a convenient and up-to-date source of the best available evidence on the role of bortezomib in the treatment of adult patients with multiple myeloma (MM) and lymphoma. The Working Group conducted a systematic review for bortezomib in patients with MM and a systematic review for bortezomib in patients with lymphoma. The evidence from these systematic reviews forms the basis of the recommendations developed by the Hematology DSG, which are available in Section 1 in the original guideline document.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Report Approval Panel Review and Approval

Prior to the submission of this Evidence-based Series (EBS) draft report for External Review, the report was reviewed and approved by the Program in Evidence-based Care (PEBC) Report Approval Panel, a panel that includes oncologists and whose members have clinical and methodological expertise.

External Review by Ontario Clinicians and Other Experts

The PEBC external review process is two-pronged and includes a targeted peer review that is intended to obtain direct feedback on the draft report from a small number of specified content experts and a professional consultation that is intended to facilitate dissemination of the final guidance report to Ontario practitioners.

Following the review and discussion of Section 1: Recommendations and Section 2: Evidentiary Base of this EBS and the review and approval of the report by the PEBC Report Approval Panel, the Hematology Disease Site Group (DSG) circulated Sections 1 and 2 to external review participants for review and feedback.

Methods

Targeted Peer Review

During the guideline development process, eight targeted peer reviewers from Ontario considered clinical and/or methodological experts on the topic were identified by the Hematology DSG. Several weeks prior to completion of the draft report, the nominees were contacted by email and asked to serve as reviewers. Three reviewers agreed, and the draft report and a questionnaire were sent via email for their review. The questionnaire consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations, and whether the draft recommendations should be approved as a guideline. Written comments were invited. The questionnaire and draft document were sent out on June 6, 2012. Follow-up reminders were sent at two weeks (email), and at four weeks (telephone call). The Hematology DSG reviewed the results of the survey.

Professional Consultation

Feedback was obtained through a brief online survey of health care professionals who are the intended users of the guideline. All hematologists, medical oncologists, pharmacists, and nurses working in Ontario and listed in the PEBC database were contacted by email to inform them of the survey. Participants were asked to rate the overall quality of the guideline (see Section 1 in the original guideline) and whether they would use and/or recommend it. Written comments were invited. Participants were contacted by email and directed to the survey website where they were provided with access to the survey, the guideline recommendations (see Section 1 in the original guideline) and the evidentiary base (see Section 2 in the original guideline). The notification email was sent on June 20, 2012. The consultation period ended on July 18, 2012. The Hematology DSG reviewed the results of the survey.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are supported by randomized and non-randomized trials.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- One randomized controlled trial (RCT) compared bortezomib plus melphalan and prednisone (n=344) to melphalan and prednisone (n=338) in patients with autologous stem cell transplantation (ASCT) ineligible, previously untreated multiple myeloma (MM). The authors reported a significantly higher median time-to-progression for the bortezomib/melphalan/prednisone arm (24.0 vs. 16.6 months; hazard ratio [HR], 0.48; $p<0.001$). Overall survival for patients who received bortezomib plus melphalan and prednisone was also higher compared to melphalan and prednisone only (at 24 months, 84% vs. 70%; HR, 0.61; $p=0.008$).
- Three RCTs of bortezomib as an induction prior to ASCT in previously untreated MM patients have been reported: two full publications and one in abstract form. One group of researchers compared induction therapy with bortezomib plus dexamethasone to vincristine, doxorubicin, and dexamethasone (VAD) prior to ASCT and found a statistically significant, better complete response and a trend toward

significance in progression-free survival in the bortezomib arm. Another group compared induction therapy with bortezomib plus dexamethasone and thalidomide to dexamethasone and thalidomide followed by a double ASCT. These authors also reported a significant and better complete remission (CR) and a better progression-free survival in the bortezomib arm.

- One RCT compared bortezomib plus pegylated liposomal doxorubicin (PLD) (n=324) to bortezomib alone (n=322) in patients with relapsed or refractory MM and reported that overall survival at 15 months was superior for the combination compared to bortezomib monotherapy (76% vs. 65%; p=0.03). The median time-to-progression was also significantly higher in the PLD plus bortezomib arm (9.3 months vs. 6.5 months, respectively; HR, 1.82; 95% confidence interval [CI], 1.41 to 2.35; p=0.000004). The Hematology Disease Site Group (DSG) opinion is that the treatment can be discontinued two to four cycles after the achievement of CR.
- One RCT compared bortezomib monotherapy (n=333) to dexamethasone (n=336) in patients with relapsed or refractory MM and reported that the median overall survival was significantly higher for patients who received bortezomib (29.8 months vs. 23.7 months; HR, 0.77; p=0.027). The median time-to-progression was also significantly higher in the bortezomib arm (HR, 0.55; p<0.001). Of note, grade 3 adverse events were more common in the bortezomib arm (61% vs. 44%; p<0.01).
- One large single-arm phase II trial was identified that investigated the use of bortezomib monotherapy in 155 patients with relapsed or refractory mantle cell lymphoma. The authors reported a median time-to-progression (TTP) of 6.7 months after a median follow-up of 26.4 months and a one-year survival of 69%.
- In newly diagnosed multiple myeloma patients, melphalan, prednisone, and bortezomib was superior in all patient subgroups to melphalan and prednisone alone. In refractory MM patients, bortezomib and dexamethasone has been shown to be superior to dexamethasone alone in patients 65 years or older (response rate p=0.0004; TTP p=0.002) and patients with International Staging System (ISS) stage II and III disease (response rate p<0.0004; TTP p=0.0002) and patients refractory to the most recent therapy or patients who have previously received greater than one prior line of therapy (response rate p<0.0001 and TTP p<0.0001 for both subgroups), as well as in patients with renal impairment. Bortezomib plus pegylated liposomal doxorubicin was also more efficacious than bortezomib alone in most subgroups analyzed. An advantage of bortezomib and pegylated liposomal doxorubicin compared to bortezomib alone was observed in patients with cytogenetic abnormalities, except for deletion 13q.

Potential Harms

- Because bortezomib is fatal if administered intrathecally, the recommendation is to administer it only by the approved intravenous or subcutaneous routes.
- *Multiple myeloma*: In all patients, bortezomib drug combinations were associated with an increased incidence of peripheral neuropathy and hematologic events, as well as nausea and diarrhea, in contrast to non-bortezomib-containing regimens (see Table 7 in Section 2 of the original guideline document for details). The Disease Site Group opinion is that blood count, blood chemistries, and creatinine levels should be monitored on days 1 and 8 of each cycle.
- *Lymphoma*: Several phase II randomized controlled trials (RCTs) of a weekly versus bi-weekly bortezomib schedule have shown an increased incidence of toxicities in the bi-weekly schedule. Cases of accidental intrathecal administration of bortezomib have been reported, and Health Canada issued an alert on January 26, 2012.

Qualifying Statements

Qualifying Statements

- Since the seminal studies on which the recommendations for patients with multiple myeloma (MM) are based were published, practice has evolved to include a weekly dosing of bortezomib. Practice has also evolved to include subcutaneous dosing of bortezomib. The Working Group considers this practice acceptable.
- Consideration should be given to the use of antiviral prophylaxis against herpes zoster (shingles) during bortezomib therapy in patients with MM. In fact, one report, in a secondary analysis of another study showed that the incidence of herpes zoster events in patients treated with bortezomib was significantly higher than in the controls who received dexamethasone alone (13% vs 5%, p=0.0002).
- The evidence provided by a phase II trial, although large, is normally considered a weak basis for recommendations. However, this group of patients has a particularly poor prognosis and have limited treatment options. Therefore, these data are considered of clinical utility.
- Responses to treatment are usually apparent by six weeks (two cycles). For patients achieving complete response (CR), bortezomib should be given for two additional cycles beyond the date of confirmed CR. In patients with progressive disease after two cycles, or stable disease after four cycles, dexamethasone (20 mg orally the day of and the day after each bortezomib dose) added to the bortezomib regimen may produce an objective response. Bortezomib (with or without dexamethasone) should be continued in patients showing benefit from therapy

(excluding those in CR), unless disease progression or significant toxicity is observed. Therapy should be discontinued in patients who do not respond to bortezomib alone if disease progression is seen within two cycles of the addition of dexamethasone.

- Lymphoma: One study suggested that bortezomib given with rituximab was better tolerated on a weekly schedule, while another study showed that, although bortezomib given alone proved to be less toxic on a weekly schedule, it provided a lower overall response than did the bi-weekly schedule. The greater ease of giving bortezomib once weekly is one more factor the Hematology Disease Site Group (DSG) Working Group considered when choosing this schedule.
- Prognostic factors (or markers) provide information about a likely disease outcome, independent of the treatment used, and can be used for risk stratification. For example, high-risk myeloma patients who do poorly with conventional treatments can be treated more aggressively, based on this risk stratification. Factors (or markers) that provide information on a disease outcome based on a specific treatment are known as predictive factors (or markers). Predictive markers can be used to identify which patients should be treated with a specific treatment. Studies on markers are under way, and the results will help in targeting specific groups of patients in the future.
- Care has been taken in the preparation of the information contained in this report. Nonetheless, any person seeking to apply or consult the report is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding the report content or use or application and disclaims any responsibility for its application or use in any way.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Kouroukis CT, Reece D, Baldassarre FG, Haynes AE, Imrie K, Cheung M, Hematology Disease Site Group. Bortezomib in multiple myeloma and lymphoma. Toronto (ON): Cancer Care Ontario (CCO); 2013 Mar 18. 209 p. (Evidence-based series; no. 6-18). [293 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2006 Apr 3 (revised 2013 Mar 18)

Guideline Developer(s)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

Guideline Developer Comment

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

Source(s) of Funding

The Program in Evidence-based Care (PEBC) is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from the Ontario Ministry of Health and Long-Term Care.

Guideline Committee

Hematology Disease Site Group

Composition of Group That Authored the Guideline

For a current list of past and present members, please see the Cancer Care Ontario Web site .

Financial Disclosures/Conflicts of Interest

The authors of this report disclosed potential conflicts of interest relating to the topic of this evidence-based series. One author (DR) was the principal investigator or the local investigator and received research funding for four trials, including one of the randomized controlled trials (RCTs) in multiple myeloma (MM) reported here. That author was also a consultant for the manufacturer of bortezomib, was an advisory board participant for a future trial, and received honoraria. One other author (TK) received honoraria while acting as a consultant for the manufacturer of bortezomib and was an advisory board participant.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Reece D, Kouroukis T, Haynes AE, Imrie K. Bortezomib in multiple myeloma and lymphoma. Toronto (ON): Cancer Care Ontario (CCO); 2008 Nov 24. 41 p. (CED-CCO special advice report; no. 11).

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Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site .

Availability of Companion Documents

The following is available:

- Program in evidence-based care handbook. Toronto (ON): Cancer Care Ontario (CCO); 2012. 14 p. Electronic copies: Available in Portable Document Format (PDF) from the CCO Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on June 29, 2006. The updated information was verified by the guideline developer on July 7, 2006. This NGC summary was updated by ECRI Institute on September 24, 2009. This summary was updated by ECRI Institute on February 26, 2010 following the U.S. Food and Drug Administration advisory on Velcade (bortezomib). This summary was updated by ECRI Institute on October 29, 2013.

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